II. The Invention

The present invention is based, in part, upon the discovery of a family of polypeptides that appear to act as a costimulator of T cell activation. In particular, the invention provides mammalian, e.g., rodent and primate polynucleotide sequences that are expressed in the thymus, and are induced on T cells and spleen cells following activation.

III. The Amendments

Claims 9-12, and 17-20 have been amended to advance and expedite prosecution by better placing the application in condition for allowance. New Claims 23-43 have been added to more particularly point out and distinctly claim the subject matter of the present invention. Certain typographical changes have been made to ensure proper antecedent basis and consistency in terminology.

Support for amending previous Claims 9-12, and 17-20 and for adding new Claim 23-43 can be found throughout the specification.

For example, support for reciting amino or nucleotide residues and specific sequence identifiers (such as in amended Claims 9, 10, 19, and 20 and new Claims 27, 29(b), 30, 32, and 33) can be found in the sequence listing for SEQ ID NO: 1-4, e.g., at pages 63-72; page 19, lines 6-16 and at page 20, lines 25-36.

Support for species, allelic and other variants as in Claims 30(b)-(c), can be found, e.g., at page 19, line 37 bridging to page 20, line 4; and at page 22, lines 10-13. Support for detectable labeling, synthetically producing, the polypeptide of the invention can be found, e.g., at page 12, lines 9-13; at page 32, lines 3-20;

Support for expression of the polypeptide of the invention on activated T cells and for binding polyclonal antibodies generated against the polypeptides of the invention can be found, e.g., at page 2, lines 21-27; page 3, lines 1-5; page 49, lines 31-34; and at page 33, lines 6-16.

Support for reciting the degeneracy of the genetic code as in new Claim 28(b) can be found, e.g., at page 7, lines 10-36.

Support for reciting natural sequences, as in new Claims 24(a-c), 30(b), and 39(b) can be found, e.g., at page 3, line 15.

Support for reciting conservative substitutions, as in new Claim 24(d)(e), 30(a), and 39(a) can be found, e.g., at page 7, line 10, bridging to page 8, line 21.

Support for reciting sequence residues to the extracellular, transmembrane and intracellular domains of SEQ ID NO: 2 or 4 as in Claim 10(a), (d) can be found, e.g., at page 4, lines 13-16 and at page 20, lines 25-36.

Support for the hybridization conditions of amended Claim 9 and new Claims 23, 30, 31, 38, and 39 can be found, e.g., page 18, lines 24-36.

Support for reciting duplex formation as in Claims 26, 33, and 34 can be found, e.g., page 58, lines 2-8; or for reciting detectable labeling can be found, e.g., page 32, line 30, bridging to page 33, line 6.

Support for the production of an antigenic polypeptide as in Claims 17, 27(d), 36, 38(b), and 42 can be found, e.g., at page 33, lines 1-10.

Support for reciting the polynucleotide of the invention in vectors and host cells as in Claims 11, 18, 34-35, and 40-41 can be found, e.g., page 4, lines 18-19; page 12, line 35, bridging to page 13, line 4; and page 38, line 14 bridging to page 40, line 2.

Support for reciting hybridization conditions as in Claims 9(a), 23, 25, 37, and 38(a) can be found, e.g., page 37, lines 16-29.

Support for reciting kits as in Claim 12 can be found, e.g., page 46, line 21 bridging to page 50, line 14.

Applicants believe that the newly added and amended claims are fully supported and introduce no new matter. Attached, for the Examiner's convenience, is a listing of the revised claims in Appendix A. Applicants believe no new issues are raised in the presently pending claims. Applicants respectfully request examination of the newly added and amended claims.

Very truly yours:

Gerald P. Keleher
P43,707

Following: draft claims

DRAFT CLAIMS FOR DISCUSSION PURPOSES ONLY

APPENDIX A: PROPOSED CLAIMS AMENDMENTS FEB-1999
GORMAN, et al.; U.S.S.N. 08/911,423; DX0612K

9. (Amended) An isolated or recombinant polynucleotide that:

a) selectively hybridizes under stringent wash conditions of at least 50° C and less than 500 mM salt to the open reading frame of SEQ ID NO: 1 or 3; and

b) encodes a polypeptide that:

i) is expressed on activated T cells; and

ii) specifically binds a polyclonal antibody generated against SEQ ID NO: 2 or 4.

10. (Amended) The polynucleotide of Claim 9, which:

a) encodes a mature polypeptide of SEQ ID NO: 2 or 4;

b) comprises the mature polypeptide coding portion of SEQ ID NO: 1 or 3;

c) comprises the extracellular domain of SEQ ID NO: 2 or 4; or

d) comprises the intracellular domain of SEQ ID NO: 2 or 4.

11. (Amended) A recombinant expression or replicating vector comprising said polynucleotide of Claim 9.

12. (Amended) A kit comprising

a) said polynucleotide of Claim 9; and

b) instructions for use or disposal of reagents in said kit.

17. (Amended) A method of producing a polypeptide, comprising expressing said vector of Claim 11, thereby producing said polypeptide.

18. (Amended) A cell comprising said vector of Claim 11.

19. (Amended) A recombinant or isolated polynucleotide of Claim 9, that encodes at least 15 contiguous amino acid residues of SEQ ID NO: 4.

20. (Amended) The polynucleotide of Claim 19, wherein said contiguous amino residues number at least 17.

23. (New) The polynucleotide of Claim 9, wherein said hybridization occurs over the entire open reading frame of SEQ ID NO: 1.

24. (New) The polynucleotide of Claim 9, wherein said polynucleotide:

a) encodes a polypeptide with a natural sequence of the mature coding portion of SEQ ID NO: 2;

b) encodes a polypeptide with a natural sequence of the mature coding portion of SEQ ID NO: 4;

c) is isolated from nature;

d) encodes a polypeptide comprising 5 or fewer conservative substitutions from a natural sequence of SEQ ID NO: 2; or

e) encodes a polypeptide comprising 5 or fewer conservative substitutions from a natural sequence of SEQ ID NO: 4.

25. (New) The polynucleotide of Claim 9, wherein said wash conditions are

a) at least 65° C;

b) less than 150 mM salt; or

c) both a) and b).

26. (New) A method of producing a polynucleotide duplex comprising contacting said polynucleotide of Claim 9 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 200 mM salt; thereby forming said duplex.

27. (New) The polynucleotide of Claim 9, which is:

a) is attached to a solid substrate;

b) is detectably labeled;

c) is in a sterile composition;

d) encodes an antigenic polypeptide having at least 12 amino acid residues; or

e) is synthetically produced.

28. (New) The polynucleotide of Claim 19, which comprises:

a) at least 57 contiguous nucleotides from the mature protein coding portion of SEQ ID NO: 1 or 3; or

b) is a variant due to the degeneracy of the genetic code.

29. (New) The polynucleotide of Claim 27, wherein:

a) said contiguous amino acid residues number at least 21; or

b) said contiguous nucleotides are from nucleotides 26-165 or nucleotides 191-241 of SEQ ID NO: 4.

30. (New) An isolated or recombinant polynucleotide encoding a polypeptide that:

a) has a conservative amino acid substitution of a mature polypeptide of SEQ ID NO: 2 or 4;

b) is a natural allelic variant of the mature native polypeptide of SEQ ID NO: 2 or 4; or

c) is a species variant of the mature native polypeptide of SEQ ID NO: 2 or 4.

31. (New) The polynucleotide of Claim 30, which is from SEQ ID NO: 4.

32. (New) The polynucleotide of Claim 30, comprising:

a) nucleotides 124 to 751 of SEQ ID NO: 1; or

b) nucleotides 54 to 723 of SEQ ID NO: 3.

33. (New) A method of producing a polynucleotide duplex comprising contacting said polynucleotide of Claim 30 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 200 mM salt; thereby forming said duplex.

34. (New) A recombinant expression or replicating vector comprising said polynucleotide of Claim 30.

35. (New) A cell comprising said vector of Claim 34.

36. (New) A method of producing an antigenic polypeptide, comprising expressing said vector of Claim 34, thereby producing said polypeptide.

37. (New) A recombinant or isolated polynucleotide that selectively hybridizes to the open reading frame of SEQ ID NO: 1 or 3 under stringent hybridization and wash conditions of at least 50°C, a salt concentration of less than 200 mM, and 50% formamide.

38. (New) The polynucleotide of Claim 37:

a) wherein said wash conditions are at least 60°C;

b) that encodes an antigenic polypeptide;

c) comprises at least 36 contiguous nucleotides of the mature coding portion of SEQ ID NO: 1 or 3; or

d) comprises at least 20 contiguous amino acids of the mature coding of SEQ ID NO: 4

39. (New) The polynucleotide of Claim 37, further encoding:

a) a two-fold or less conservative amino acid substitution of a mature polypeptide of SEQ ID NO: 2 or 4;

b) a natural allelic variant of the native polypeptide of SEQ ID NO: 2 or 4; or

c) a species variant of the native polypeptide of SEQ ID NO: 2 or 4.

40. (New) A recombinant expression or replicating vector comprising:

a) said polynucleotide of Claim 37; or

b) the mature polypeptide of SEQ ID NO: 4.

41. (New) A cell comprising said vector of Claim 40.

42. (New) A method of producing an antigenic polypeptide, comprising expressing said vector of Claim 41, thereby producing said polypeptide.

43. (New) A method of producing a polynucleotide duplex comprising contacting said polynucleotide of Claim 37 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 200 mM salt; thereby forming said duplex.